(19) World Intellectual Property Organization International Bureau



Į.

(43) International Publication Date 15 January 2004 (15.01.2004)

PCT

(10) International Publication Number WO 2004/005466 A3

- (51) International Patent Classification⁷: G01N 33/53, 33/574, 33/543, 33/577, A61B 5/055, A61K 49/16, C12Q 1/68
- (21) International Application Number:

PCT/US2003/020841

(22) International Filing Date:

3 July 2003 (03.07.2003)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: 60/393,982

3 July 2002 (03.07.2002) US

- (71) Applicant (for all designated States except US): ILLUMI-GEN BIOSCIENCES [US/US]; 2203 Airport Way South, Suite 450, Seattle, WA 98134-2028 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): KATZE, Michael [US/US]; 200 West Mercer Street, Suite E-412, Seattle, WA 98119 (US). BUMGARNER, Roger [US/US]; 200 West Mercer Street, Suite E-412, Seattle, WA 98119 (US). SMIT, Maria [US/US]; 200 West Mercer Street, Suite E-412, Seattle, WA 98119 (US). ROSENBURG, Gary [US/US]; 200 West Mercer Street, Suite E-412, Seattle, WA 98119 (US).

- (74) Agents: CONFORTI, Vita, G. et al.; Davis Wright Tremaine LLP, 2600 Century Square, 1501 Fourth Avenue, Seattle, WA 98101-1688 (US).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- (88) Date of publication of the international search report: 26 August 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHODS AND COMPOSITIONS FOR DIAGNOSING HEPATOCELLULAR CARCINOMA

(57) Abstract: Methods for the diagnosis of hepatocellular carcinoma (HCC) are set forth. Improved assay methods and scanning methods are included that employ non-cell-associated and cell-associated HCC related proteins. Such methods are based upon the discovery of genes that were up-regulated in diseased versus normal tissue as well as in HCC tissue when compared to the tissue of patients with other ailments.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/20841

A. CLASSIFICATION OF SUBJECT MATTER								
IPC(7) : G01N 33/53, 33/574, 33/543, 33/577; A61B 5/055; A61K 49/16; C12Q 1/68 US CL : 435/6, 7.1, 7.23, 7.93, 15; 424/9.1, 9.34								
According to International Patent Classification (IPC) or to both national classification and IPC								
B. FIELDS SEARCHED								
Minimum documentation searched (classification system followed by classification symbols) U.S.: 435/6, 7.1, 7.23, 7.93, 15; 424/9.1, 9.34								
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched								
Electronic data base consulted during the international search (name of data base and, where practicable, search Please See Continuation Sheet	ch terms used)							
C. DOCUMENTS CONSIDERED TO BE RELEVANT								
Category * Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.							
X LIN et al. Clinical Aspects of Hepatoceullular Carcinoma: Role of Serum C-Reactive Protein as a Marker of Hepatocellular Carcinoma in Patients with Cirrhosis. Journal of Gastroenterology and Hepatology. 2000, Vol. 15, pages 417-421, especially.	1-4, 6-9							
X TROJAN et al. Fluorine-18 FDG Position Emission Tomography for Imaging of Hepatocellular Carcinoma. Am. J. Gastroenterol., November 1999, Vol. 94, pages 3314-3319, especially.	1-4, 6-9, 11, 14, 16							
X TAKAHASHI et al. Expression of Telomerase Component Genes in Hepatocellular Carcinoma. Eur. J. Cancer. March 2000, Vol. 36, pages 496-502, especially page 497.	15							
A SMITH et al. Identification of Novel Tumor Markers in Hepatitis C Virus-Associated Hepatocellular Carcinoma. Cancer Research. February 2003, Vol. 63, pages 859-864.	5, 10, 12-13							
Further documents are listed in the continuation of Box C. See patent family annex.								
Special categories of cited documents:	ation but cited to understand the							
"A" document defining the general state of the art which is not considered to be principle or theory underlying the inve of particular relevance								
"E" earlier application or patent published on or after the international filing date "E" document of particular relevance; the considered novel or cannot be considered when the document is taken alone								
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as "Y" document of particular relevance; the considered to involve an inventive step combined with one or more other such	when the document is							
"O" document referring to an oral disclosure, use, exhibition or other means being obvious to a person skilled in the	e art							
"P" document published prior to the international filing date but later than the "&" document member of the same patent priority date claimed	•							
Date of the actual completion of the international search Date of mailing of the international search	ch report							
29 May 2004 (29.05.2004)								
Name and mailing address of the ISA/US Mail Stop PCT, Atm: ISA/US MISONS THE Ph.D. Name of the ISA/US	exce In							
Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Telephone No. 571-272-1600	FUP							

Form PCT/ISA/210 (second sheet) (July 1998)

	INTERNATIO	DNAL SEARCI	AEFORT				
							·
					-		
Continua	tion of B. FIELDS	SEARCHED Ite	em 3:				•
Dialog (5, Search terr SPECT, R	tion of B. FIELDS 155), and West (USP) ns: hepatocellular can T-PCR.	SEARCHED Ite F, DWPI) cinoma, ELISA, se	em 3: created protein,	antibody, PLA	A2G13, phospholip	pase A2, in vivo i	maging, MRI, CT,
Continua Dialog (5, Search terr SPECT, R	tion of B. FIELDS 155), and West (USP ns: hepatocellular can T-PCR.	SEARCHED Ite I, DWPI) cinoma, ELISA, se	em 3: created protein,	antibody, PLA	A2G13, phospholiq	pase A2, in vivo i	maging, MRI, CT,
Dialog (5, Search terr SPECT, R	tion of B. FIELDS 155), and West (USP ns: hepatocellular care T-PCR.	SEARCHED Ite F, DWPI) cinoma, ELISA, se	em 3: created protein,	antibody, PLA	A2G13, phospholiq	pase A2, in vivo i	
Dialog (5, Search terr SPECT, R	tion of B. FIELDS 155), and West (USP ns: hepatocellular can T-PCR.	SEARCHED Ite F, DWPI) Sinoma, ELISA, se	em 3: created protein,	antibody, PLA	A2G13, phospholip	pase A2, in vivo i	
Dialog (5, Search terr SPECT, R	tion of B. FIELDS 155), and West (USP ns: hepatocellular care T-PCR.	SEARCHED Ite F, DWPI) Sinoma, ELISA, se	em 3: created protein,	antibody, PLA	A2G13, phospholip	pase A2, in vivo i	
Dialog (5, Search terr SPECT, R	tion of B. FIELDS 155), and West (USP ns: hepatocellular care T-PCR.	SEARCHED Ite F, DWPI) Sinoma, ELISA, se	em 3: created protein,	antibody, PLA	A2G13, phospholip	pase A2, in vivo i	
Dialog (5, Search terr SPECT, R	tion of B. FIELDS 155), and West (USP ns: hepatocellular care T-PCR.	SEARCHED Ite F, DWPI) Sinoma, ELISA, se	em 3: created protein,	antibody, PLA	A2G13, phospholip	pase A2, in vivo i	
Dialog (5, Search terr SPECT, R	tion of B. FIELDS 155), and West (USP ns: hepatocellular care T-PCR.	SEARCHED Ite F, DWPI) cinoma, ELISA, se	created protein,	antibody, PLA		pase A2, in vivo i	
Dialog (5, Search terr SPECT, R	tion of B. FIELDS 155), and West (USP ns: hepatocellular care T-PCR.	SEARCHED Ite F, DWPI) cinoma, ELISA, se	created protein,			pase A2, in vivo i	

PCT/US03/20841

Form PCT/ISA/210 (second sheet) (July 1998)